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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/757,774	01/09/2001	Howard M. Dintzis	07265-124005	8467

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EXAMINER

SAUNDERS, DAVID A

ART UNIT	PAPER NUMBER
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1644

DATE MAILED: 04/09/2003

60

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

757,774

Applicant(s)

DINTZIS et al

Examiner

SAUNDER

Group Art Unit

1644

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

- ☒ Responsive to communication(s) filed on 12/26/01
- ☐ This action is FINAL.
- ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

- ☒ Claim(s) 44-87 is/are pending in the application.
- Of the above claim(s) 70-87 is/are withdrawn from consideration.
- ☐ Claim(s) is/are allowed.
- ☒ Claim(s) 44-69 is/are rejected.
- ☐ Claim(s) is/are objected to.
- ☐ Claim(s) are subject to restriction or election requirement.

Application Papers

- ☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
- ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

- ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
 - ☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been received.
 - ☐ received in Application No. (Series Code/Serial Number) _____.
 - ☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____

Attachment(s)

- ☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
- ☒ Notice of Reference(s) Cited, PTO-892
- ☐ Notice of Draftsperson's Patent Drawing Review, PTO-948
- ☐ Interview Summary, PTO-413
- ☐ Notice of Informal Patent Application, PTO-152
- ☐ Other _____

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Claims 44-87 are pending.

Applicant's election without traverse of Group I (claims 44-49) in Paper No. 9 is acknowledged.

The disclosure is objected to because of the following informalities: the status of each referenced application (e.g. page 22, lines 17 and 18) must be updated.

Appropriate correction is required.

Claims 44-68 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 44, lines 8-9 "the size-fractioned non-immunogenic soluble carrier" lacks antecedent basis, because step (a) has recited "preparative sizing technique" rather than "sizing - fractionation."

Claims 44-69 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: Claims 44 and 69 leave out a step, after the "coupling" of step (b), of further size fractionating the conjugated preparation. Applicant's disclosure has taught that such a post-conjugation size-fractionation is necessary. See page 77, line 29 - page 78, line 10.

Claims 44-69 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one

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skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims contain new matter.

Claims 44 and 69 recite new matter because after the "coupling" step (b) there is no additional step of further size fractionating the conjugate preparation. The examiner finds that the original disclosure describes and requires such a post-conjugation size fractionating step; see page 77, line 29 - page 78, line 10 and page 104, lines 22-25, as well as original claims 14-16.

Claim 58 contains new matter by reciting "about 20,000 daltons." The examiner cannot find 20,000 recited in the original disclosure. Please point out support by page and line number;. Also point out basis for recitation of "about" with this value.

For claim 63, the examiner cannot find where the original disclosure recites "4" or "30" and, if so, where there is basis for reciting "about" with each of these numbers.

In like manner the examiner cannot determine where there is support for reciting "about 6 to about 14" in claim 64.

Regarding claim 65, the examiner notes that "20" is recited at page 23, line 4 and page 111, line 28. However there is no basis therein for reciting "about" in conjunction with "20."

Claim 67 contains new matter because the examiner finds no teaching that the instantly provided conjugates are "immunosuppressive to t-cells." While applicant teaches that these conjugates suppress T-dependent responses. This is not a teaching that the T-cells per se are suppressed.

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Claims 44-69 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Step (b) of claims 44 and 69 is not enabled without the conducting of a post-coupling step which further size fractionate the conjugate preparation.

Applicant's disclosure states that this step is necessary because the conjugation reactions unavoidably have associated side-reactions between polymer molecules which yield conjugates of excessive molecular weight. See page 77, line 29 - page 78, line 10. Since applicant has not taught how to avoid such side reactions, it would require undue experimentation for one to provide a non-immunogenic construct, without conducting a post conjugation size-fractionation step.

Claim 67 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The specification does not teach how to render the non-immunogenic construct "immunosuppressive to T-cells".

The examiner finds no such teaching regarding T-cells in the disclosure. Also, Barstad et al. teach conjugates of essentially the same composition, and they teach that these conjugates induce "B-cell anergy (unresponsiveness)" at col. 2, lines 58+, rather than T-cell anergy/suppression. Also applicant's own teachings of the immunon/clustering model

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indicates that the immunosuppressive effects occur at the B-cell, not the T cell surface. Thus one would not expect the instant conjugates to immunosuppress T-cells.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 44, 52-53, 56, 59-60 and 66-69 are rejected under 35 U.S.C. 102(b) as being anticipated by Applicant's admitted state of the art at pages 6-10.

Applicant has admitted that other workers, e.g. Katz, Diener, have coupled haptens to non-immunogenic soluble carriers that have a molecular weight appropriate for inducing tolerance, anergy, or immunosuppression. Katz used poly (D-Glu, D-Lys) of

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M.w. less than 100 KDa (100,000 d). Likewise applicant notes that Diener employed a CM-cellulose carrier of less than 100 kda.

It is apparent that applicant considers the immunosuppressive effects of these prior art conjugates to have been fortuitously discovered, because the prior workers did not recognize the necessity of using a soluble polymeric carrier of less than 100 kda. See page 10. However, these prior art polymers, as purchased or prepared by the workers did not contain "high molecular weight non-immunogenic soluble carrier molecules" (as recited in instant step (a)). Irrespective of how these polymers were prepared and whether or not they had been size fractionated prior to coupling of the haptens, these prior art polymer preparations had the same composition that applicant teaches as being appropriate for practicing the instant invention. As such the components that applicant provides in step (a), as the two reactants for step (b), is the same as what the prior art provided, irrespective of what method did or did not provide the starting materials. What enters into the coupling reaction of step (b) is thus the same as what entered into the coupling/conjugation reactions of the prior art. Applicant's claimed method steps of claims 44 and 69 are thus anticipated.

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What applicant has admitted as known in the prior art is consistent with the limitations of instant dependent claims 52-53, 56, and 66-68.

Dependent claims 59-60, while they recite sizing methods, are included because the examiner has taken the position that the history of preparation of the starting materials of step (a) is not relevant as long as the polymer has an appropriate molecular weight range.

Claims 44-46, 49, 50-53, 59-61, and 63-69 are rejected under 35 U.S.C. 102(e) as being anticipated by Barstad et al. (5,268,454).

Barstad et al. teach the induction of humoral anergy/unresponsiveness/tolerance/immunosuppression by administering conjugates of epitopic analogs coupled to a D-EK polymer carrier of 5,000-30,000 daltons --e.g. see col. 5, lines 47-51. Following the position taken in the above rejection, the examiner considers this polymeric starting material of Barstad et al. to not be materially different as a composition from what applicant provides in step (a). Claims 44, and 66-69 are thus anticipated.

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Claims 52-53 are anticipated because the D-EK polymer of Barstad et al. is the same as what applicant recites in claim 53. See col. 5, lines 12-16.

Regarding claims 45-46 and 49 note col. 3, lines 55-69 and Example 1.

For claims 50-51, note claims 3-4 of Barstad et al.

The 5,000 to 30,000 dalton carrier used by Barstad et al. is consistent with instant claims 56-57.

Claims 59-60 are included because the history of the polymers preparation is not material.

Concerning claim 61, the bifunctional linker taught at col. 5 and in the Examples provide a "spacer".

Regarding claims 63-65, note col. 5, line 49.

Claims 44, 47, 50-53, 56-57, 59-60 and 66-69 are rejected under 35 U.S.C. 102(b) as being anticipated by Katz (4,191,668).

The teachings of Katz correspond to those which applicant has admitted (pages 6-10) as prior art. The claims are thus rejected following the same rational as that stated supra, based on applicant's admissions. Regarding dependent claim 50, BPO is a hapten (epitope) "derived" from an allergen. See col. 4, line 55 - col. 5, line 5, line 20 and col. 6, lines 45 - col. 7, line 9. Regarding claims 47 and 51, note col. 10, lines 15-68.

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Applicant should recite claims such that size fractionation step is actually conducted in step (a).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Saunders, Ph.D., whose telephone number is (703) 308-3976. The examiner can normally be reached on Monday-Thursday from 8:00 a.m. to 5:30 p.m. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached on (703) 308-3973. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

D. Saunders:jmr

March 28, 2003

David A. Saunders
DAVID SAUNDERS
PRIMARY EXAMINER
ART UNIT 1644